# Variation in Mammographic Breast Density Assessments Among Radiologists in Clinical Practice

## A Multicenter Observational Study

**Brian L. Sprague, PhD; Emily F. Conant, MD; Tracy Onega, PhD; Michael P. Garcia, MS; Elisabeth F. Beaber, PhD; Sally D. Herschorn, MD; Constance D. Lehman, MD, PhD; Anna N.A. Tosteson, ScD; Ronilda Lacson, MD, PhD; Mitchell D. Schnall, MD, PhD; Despina Kontos, PhD; Jennifer S. Haas, MD, MSc; Donald L. Weaver, MD; and William E. Barlow, PhD; on behalf of the PROSPR Consortium**

**Background:** About half of U.S. states currently have legislation requiring radiology facilities to disclose mammographic breast density information to women, often with language recommending discussion of supplemental screening options for women with dense breasts.

**Objective:** To examine variation in breast density assessment across radiologists in clinical practice.

**Design:** Cross-sectional and longitudinal analyses of prospectively collected observational data.

**Setting:** 30 radiology facilities within the 3 breast cancer screening research centers of the Population-based Research Optimizing Screening through Personalized Regimens (PROSPR) consortium.

**Participants:** Radiologists who interpreted at least 500 screening mammograms during 2011 to 2013 ($n$ = 83). Data on 216 783 screening mammograms from 145 123 women aged 40 to 89 years were included.

**Measurements:** Mammographic breast density, as clinically recorded using the 4 Breast Imaging Reporting and Data System categories (heterogeneously dense and extremely dense categories were considered "dense" for analyses), and patient age, race, and body mass index (BMI).

**Results:** Overall, 36.9% of mammograms were rated as showing dense breasts. Across radiologists, this percentage ranged from 6.3% to 84.5% (median, 38.7% [interquartile range, 28.9% to 50.9%]), with multivariable adjustment for patient characteristics having little effect (interquartile range, 29.9% to 50.8%). Examination of patient subgroups revealed that variation in density assessment across radiologists was pervasive in all but the most extreme patient age and BMI combinations. Among women with consecutive mammograms interpreted by different radiologists, 17.2% (5909 of 34 271) had discordant assessments of dense versus nondense status.

**Limitation:** Quantitative measures of mammographic breast density were not available for comparison.

**Conclusion:** There is wide variation in density assessment across radiologists that should be carefully considered by providers and policymakers when considering supplemental screening strategies. The likelihood of a woman being told she has dense breasts varies substantially according to which radiologist interprets her mammogram.

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For author affiliations, see end of text.
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* For a list of PROSPR investigators and research staff, see the Appendix (available at www.annals.org).

Mammographic breast density impairs mammography performance and is also an independent risk factor for breast cancer (1, 2). To ensure that women with dense breasts are aware of the limitations of mammography and their increased breast cancer risk, about half of U.S. states currently have legislation mandating the disclosure of breast density information directly to women (3). In many states, these notifications are required to include language advising the woman to discuss supplemental screening tests with her providers if her breasts are considered to be dense (4, 5). National legislation is currently under consideration (6), and the U.S. Food and Drug Administration is also considering an amendment to its regulations issued under the Mammography Quality Standards Act that would require reporting of density information to patients (7).

These legislative and regulatory initiatives have generated controversy because of the large number of women affected and the lack of evidence or consensus in the medical community with regard to appropriate supplemental screening strategies for women with dense breasts. Approximately 40% of U.S. women aged 40 to 74 years have dense breast tissue based on mammographic assessment (8). Ultrasonography, digital breast tomosynthesis, and magnetic resonance imaging have been proposed as screening options for women with dense breasts, but there is limited evidence to support the comparative effectiveness of these approaches for an indication of breast density alone (9).

An additional prominent concern with breast density legislation is the subjective nature of breast density assessment as routinely practiced in the clinical setting (10). Radiologists classify the appearance of the overall breast composition on a mammogram by using the Breast Imaging Reporting and Data System (BI-RADS) lexicon (11, 12), which includes 4 categories: almost entirely fat, scattered fibroglandular densities, heterogeneously dense, or extremely dense, with the latter 2

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categories considered "dense" in existing legislation. Prior studies using test sets or consecutive mammograms have reported substantial intrarater and interrater variability in radiologists' measurements of BI-RADS breast density, with κ statistics ranging from 0.4 to 0.7 (13–17). The effect of this variability on the distribution of mammographic breast density measurements in clinical practice is not clear, particularly in relation to individual patient determinants of breast density, such as age and body mass index (BMI) (8).

We sought to examine variation in the distribution of breast density assessments across radiologists as recorded in clinical practice while accounting for patient factors known to be associated with breast density. We used data from 30 radiology facilities within the 3 breast cancer screening research centers of the Population-based Research Optimizing Screening through Personalized Regimens (PROSPR) consortium. Our results will inform debates about the appropriateness of relying on subjective breast density assessment in clinical decision making and have implications for personalized screening recommendations while also providing comparison data for radiologists to assess how their density assessment practice compares with that of their peers.

## METHODS

### Setting

This study was conducted as part of the National Cancer Institute–funded PROSPR consortium. The overall aim of PROSPR is to conduct multisite, coordinated, transdisciplinary research to evaluate and improve cancer screening processes. The 10 PROSPR research centers reflect the diversity of U.S. delivery system organizations (18). We used data from the 3 PROSPR breast cancer screening research centers: an integrated health care delivery system affiliated with the University of Pennsylvania, a statewide mammography and pathology registry housed at the University of Vermont, and primary care practice networks in 2 states affiliated with the Dartmouth-Hitchcock health system in New Hampshire and Brigham and Women's Hospital in Massachusetts.

### Study Design

We conducted an observational study using prospectively collected data from routine clinical practice. No interventions or training related to breast density assessment were introduced as part of the study. Each PROPSR breast cancer screening research center collects comprehensive clinical data on breast cancer screening among its catchment population. In total, the 3 centers capture mammography data from 30 radiology facilities. Cross-sectional and longitudinal analyses of the observational data were performed, as detailed in the Statistical Analysis section. All activities were approved by the institutional review boards at each PROSPR research center and the PROSPR Statistical Coordinating Center.

### Participants and Mammograms

We identified all records of screening mammography conducted during 2011 to 2013 among women aged 40 to 89 years (*n* = 269 741 examinations). The study period was before density notification legislation was enacted in the 4 included states. Mammographies were eligible on the basis of 2 requirements: the indication for the examination was screening (as provided by the radiology facility), and no breast imaging was done within the 3 months before the examination (to avoid inclusion of diagnostic examinations that may have been miscoded as screening examinations). We then applied the following exclusion criteria: mammograms missing a breast density assessment (*n* = 31 232), examinations conducted among women with a history of breast cancer (*n* = 9337), mammograms missing a radiologist identification number (*n* = 5629), and mammograms interpreted by radiologists who interpreted fewer than 500 screening mammograms included in the database during the study period (*n* = 6760 examinations among 48 radiologists). From an initial sample that included 171 549 women with screening mammograms during 2011 to 2013, the final sample included 145 123 women.

### Data Collection

Common data elements to ascertain patient characteristics and mammography data were developed by the PROSPR research centers and Statistical Coordinating Center. Patient characteristics (including age, race, BMI, and history of breast cancer) at the time of the examination were obtained via a radiology clinic patient questionnaire (at the University of Pennsylvania and University of Vermont facilities) or from the patient's electronic medical record (in the Dartmouth/Brigham and Women's Hospital network). Other details of the examination were also obtained directly from the radiology facilities, including date of the examination; identification number of the interpreting radiologist; and descriptor of mammographic breast density, which was clinically recorded using the BI-RADS lexicon (almost entirely fat, scattered fibroglandular densities, heterogeneously dense, or extremely dense [11]). Descriptions that did not use the BI-RADS lexicon were excluded as missing. Data from the 3 PROSPR breast cancer research centers were submitted to the PROSPR central data repository, which is housed at the Statistical Coordinating Center at the Fred Hutchinson Cancer Research Center.

### Statistical Analysis

All statistical analyses were performed using SAS, version 9 (SAS Institute), and R, version 3.2.0 (R Foundation for Statistical Computing). Descriptive statistics were used to describe the distribution of patient characteristics in the study sample and the raw distribution of breast density assessments across radiologists. For certain analyses, breast density assessments were dichotomized as nondense (almost entirely fat or scattered fibroglandular densities) or dense (heterogeneously or extremely dense) according to the definitions used in density notification laws in most

*Table 1.* Characteristics of the Study Population*

| Characteristic | Participants (*n* = 145 123), *n* (%) |
|---|---|
| **Age** | |
| 40–49 y | 39 222 (27.0) |
| 50–59 y | 47 525 (32.8) |
| 60–69 y | 37 108 (25.6) |
| 70–89 y | 21 268 (14.7) |
| **Race/ethnicity** | |
| Non-Hispanic white | 115 905 (79.9) |
| Non-Hispanic African American | 14 532 (10.0) |
| Non-Hispanic Asian/Pacific Islander | 2632 (1.8) |
| Non-Hispanic other | 2963 (2.0) |
| Hispanic | 5812 (4.0) |
| Unknown | 3279 (2.3) |
| **Body mass index** | |
| <18.5 kg/m$^2$ | 3082 (2.1) |
| 18.5–24.9 kg/m$^2$ | 47 855 (33.0) |
| 25.0–29.9 kg/m$^2$ | 38 508 (26.5) |
| 30.0–34.9 kg/m$^2$ | 22 486 (15.5) |
| ≥35.0 kg/m$^2$ | 18 648 (12.9) |
| Unknown | 14 544 (10.0) |
| **PROSPR research center** | |
| Dartmouth/Brigham and Women's Hospital | 32 104 (22.1) |
| University of Pennsylvania | 33 975 (23.4) |
| University of Vermont | 79 044 (54.5) |

PROSPR = Population-based Research Optimizing Screening through Personalized Regimens.
* At first screening mammography during the study period. A total of 52 800 women contributed multiple examinations to the study. Percentages may not sum to 100 due to rounding.

states (5). To account for variation in patient characteristics across radiologists, we fit a logistic regression model of breast density to the patients for each radiologist, adjusting for patient age, race/ethnicity, and BMI (categorized as shown in Table 1). A total of 24 816 examinations with missing race/ethnicity or BMI were excluded from the multivariable analyses (11.4% of the total sample). The models were used to estimate adjusted percentages of mammograms categorized as showing dense breasts, which were standardized to the joint age and BMI distribution in the overall study population (19). This procedure estimated the percentage of mammograms each radiologist would classify as showing dense breasts if each radiologist's patients had the same distribution of age, race/ethnicity, and BMI as in the entire population. The difference between the unadjusted percentage of dense ratings and the estimated percentage of dense ratings weighted to a standard population is shown in the Appendix Figure (available at www.annals.org). Some women contributed multiple screening examinations during the study period. Results were similar when we accounted for clustering of density assessments due to multiple examinations per woman by using generalized estimating equations with an independent working correlation structure. Therefore, we used the simpler logistic regression model.

Data on consecutive screening examinations were available for 45 313 women. We compared the density assessments from the first 2 available consecutive examinations per patient, with stratification according to whether the mammograms were interpreted by the same radiologist or different ones. A chi-square test was used to determine whether the discordance in dense versus nondense ratings on consecutive examinations differed when the mammograms were interpreted by the same radiologist versus different ones.

## Role of the Funding Source

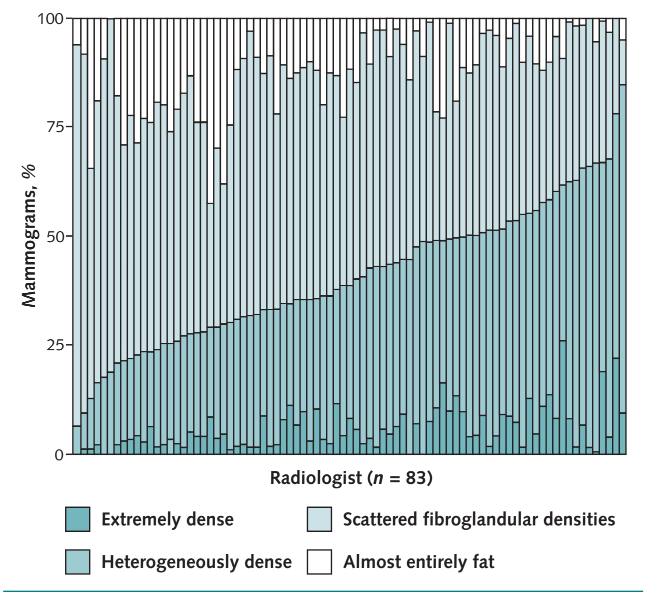
This work was funded by the National Cancer Institute. The funding source had no role in the design of the study; the collection, analysis, and interpretation of the data; or the approval of the final version of the manuscript.

## RESULTS

The final study population for analysis consisted of 216 783 screening mammograms from 145 123 women, which were interpreted by 83 radiologists (16 from the University of Pennsylvania site, 39 from the University of Vermont site, and 28 from the Dartmouth/Brigham and Women's Hospital site). The mean age of the patient population was 57.9 years (SD, 10.8 years; median, 57.0 years; range, 40 to 89 years). Approximately 80% of patients were non-Hispanic white, and more than half were overweight or obese (Table 1). Overall, 36.9% of mammograms were rated as showing dense breasts (heterogeneously or extremely dense).

Use of the 4 breast density categories varied substantially across radiologists (Figure). The median percentage of mammograms rated as showing dense breasts (heterogeneously or extremely dense) was

*Figure.* Distribution of BI-RADS breast density assessments, by radiologist.




The radiologists are arranged in ascending order of the percentage of mammograms rated as showing dense breasts (heterogeneously or extremely dense). BI-RADS = Breast Imaging Reporting and Data System.

*Table 2.* Distribution of Breast Density Assessment Categories Among 83 Radiologists and 216 783 Screening Mammograms, as Interpreted During Routine Clinical Practice

| Density Assessment | Radiologists, *n* | Median Mammograms in Each Density Category (Range; Interquartile Range), %* |
|---|---|---|
| **All centers** | 83 | – |
| Almost entirely fat | – | 10.9 (0.0–42.6; 4.3–19.3) |
| Scattered fibroglandular densities | – | 48.3 (10.3–87.7; 37.1–54.1) |
| Heterogeneously dense | – | 33.8 (6.1–75.3; 24.2–44.6) |
| Extremely dense | – | 4.0 (0.0–25.8; 1.9–8.5) |
| Heterogeneously or extremely dense | – | 38.7 (6.3–84.5; 28.9–50.9) |
| **Heterogeneously or extremely dense, by center** | | |
| Dartmouth/Brigham and Women's Hospital | 28 | 44.1 (21.7–67.5; 37.2–52.1) |
| University of Pennsylvania | 16 | 47.9 (23.6–66.6; 31.8–55.6) |
| University of Vermont | 39 | 30.1 (6.3–84.5; 24.2–46.7) |

* For each density category, we computed the percentage of examinations that each radiologist classified in that category. The distribution of these 83 percentages is then described using the median, range (minimum–maximum), and interquartile range (25th–75th percentile). For example, the median percentage of examinations in the heterogeneously dense category among the 83 radiologists was 33.8%. The range indicates that 1 radiologist rated only 6.1% of examinations as heterogeneously dense, whereas another rated 75.3% as such. Twenty-five percent of the radiologists rated ≤24.2% of their examinations as heterogeneously dense, whereas the top quartile rated ≥44.6% as such.

38.7%, with an interquartile range of 28.9% to 50.9% and a full range of 6.3% to 84.5% (**Table 2**). Twenty-five percent of radiologists rated fewer than 28.9% of their patients' mammograms as showing dense breasts, whereas the highest 25% of radiologists rated at least 50.9% of their patients' mammograms as showing dense breasts. Among the 4 specific density categories, the absolute degree of variation was widest for the heterogeneously dense category, with an interquartile range of 24.2% to 44.6% across radiologists. Variation was markedly lower for the extremely dense category (interquartile range, 1.9% to 8.5%).

Stratification by PROSPR center revealed substantial variation in density assessment across radiologists within each center (**Table 2**). The full range was widest at the University of Vermont site and centered on a lower median than at the University of Pennsylvania and Dartmouth/Brigham and Women's Hospital sites.

Multivariable adjustment for patient age, race, and BMI had little effect on the variation across radiologists in the percentage of mammograms rated as showing dense breasts (**Appendix Figure**). After adjustment, the median was 40.1% and the interquartile range was 29.9% to 50.8%.

Stratification by patient age and BMI revealed substantial variation across radiologists in the percentage of mammograms rated as showing dense breasts within nearly all age and BMI categories (**Table 3**). Among women with a BMI of 18.5 to 24.9 kg/m$^2$, density assessments varied widely across radiologists among both younger women (interquartile range, 64% to 85% for women aged 40 to 49 years) and older women (interquartile range, 38% to 63% for women aged 60 to 69 years).

For women with consecutive examinations during the study period, the mean time between the first and second examinations was 1.2 years both for women with mammograms interpreted by different radiologists (median, 1.1 years [interquartile range, 1.0 to 1.3 years]) and for women with mammograms interpreted by the same radiologist (median, 1.1 years [interquartile range, 1.0 to 1.2 years]). Among women with consecutive mammograms interpreted by different radiologists (*n* = 34 271 women), 32.6% had a different density assessment at the 2 examinations (**Table 4**). The most common changes were from heterogeneously dense to scattered fibroglandular densities (9.6%) and vice versa (6.8%). With density dichotomized as dense or nondense, 17.2% of women with consecutive mammograms interpreted by different radiologists had discordant density ratings at the 2 examinations (**Table 4**); 27.0% of women with dense breasts at the first examination were deemed to have nondense breasts at the second examination, and 11.4% of women with nondense breasts at the first examination were deemed to have dense breasts at the second examination. The discordance rate for dense versus nondense status was significantly smaller when consecutive mammograms were interpreted by the same radiologist versus different ones (chi-square = 645 [1 degree of freedom]; $P < 0.001$). Among women with consecutive mammograms interpreted by the same radiologist (*n* = 11 042 women), 10.0% had discordant ratings for dense versus nondense status at the 2 examinations.

## DISCUSSION

Our findings show wide variation among radiologists in the percentage of mammograms rated as showing dense breasts (ranging from 6.3% to 84.5% in our sample), which persisted after adjustment for patient factors. In addition, 17.2% of women (more than 1 in 6) with consecutive mammograms interpreted by different radiologists during a short period were reclassified into dense versus nondense categories. This variation has important implications for debates about mandatory reporting of density information, clinical management of patients who are told they have dense breasts, and investigators using radiologists' subjective measures of breast density in cancer research.

The widespread enactment of breast density notification laws presents physicians with the challenging

***Table 3.*** Distribution of Percentage of Mammograms Rated as Showing Heterogeneously or Extremely Dense Breasts, Stratified by Age and Body Mass Index

| BMI, by Age | Sample Size (Mammograms), *n* | Radiologists, *n*† | Median Mammograms Rated as Showing Dense Breasts (Range; Interquartile Range), %* |
|---|---|---|---|
| **Women aged 40–49 y** | | | |
| <18.5 kg/m² | 1201 | 82 | 88 (36–100; 81–94) |
| 18.5–24.9 kg/m² | 20 028 | 83 | 77 (16–97; 64–85) |
| 25.0–29.9 kg/m² | 13 233 | 83 | 54 (8–90; 38–69) |
| 30.0–34.9 kg/m² | 7445 | 83 | 39 (2–91; 23–54) |
| ≥35.0 kg/m² | 6789 | 83 | 19 (1–71; 11–33) |
| **Women aged 50–59 y** | | | |
| <18.5 kg/m² | 1425 | 82 | 80 (29–100; 69–88) |
| 18.5–24.9 kg/m² | 24 247 | 83 | 63 (12–94; 51–75) |
| 25.0–29.9 kg/m² | 18 648 | 83 | 40 (6–84; 28–55) |
| 30.0–34.9 kg/m² | 10 764 | 83 | 25 (2–72; 15–38) |
| ≥35.0 kg/m² | 9073 | 83 | 11 (1–51; 6–22) |
| **Women aged 60–69 y** | | | |
| <18.5 kg/m² | 1118 | 83 | 72 (16–100; 58–81) |
| 18.5–24.9 kg/m² | 18 177 | 83 | 50 (6–91; 38–63) |
| 25.0–29.9 kg/m² | 15 918 | 83 | 27 (3–77; 18–40) |
| 30.0–34.9 kg/m² | 9405 | 83 | 16 (1–62; 9–27) |
| ≥35.0 kg/m² | 7339 | 83 | 7 (0–38; 4–15) |
| **Women aged 70–89 y** | | | |
| <18.5 kg/m² | 849 | 81 | 62 (8–98; 46–75) |
| 18.5–24.9 kg/m² | 10 740 | 83 | 40 (3–90; 26–54) |
| 25.0–29.9 kg/m² | 10 212 | 83 | 19 (1–75; 12–30) |
| 30.0–34.9 kg/m² | 5452 | 83 | 11 (0–59; 6–20) |
| ≥35.0 kg/m² | 3003 | 83 | 5 (0–32; 2–11) |

BMI = body mass index.
* Includes those rated as showing heterogeneously dense and extremely dense breasts. Adjusted for patient race/ethnicity.
† Radiologists who interpreted <5 mammograms in a given age/BMI category were excluded from statistics for that category.

task of discussing the potential benefits and harms of supplemental breast cancer screening in the absence of consensus guidelines (10). Overall, our findings suggest that a woman's likelihood of being told she has dense breasts varies substantially on the basis of which radiologist interprets her mammogram. Primary care providers should therefore use caution when considering supplemental breast cancer screening options for a

***Table 4.*** Breast Density Assessment Among Women With 2 Consecutive Examinations During the Study Period*

| Density at First Examination | Density at Second Examination | | | | Total |
|---|---|---|---|---|---|
| | Almost Entirely Fat | Scattered Fibroglandular Densities | Heterogeneously Dense | Extremely Dense | |
| **All women** | | | | | |
| Almost entirely fat | 4877 (10.8) | 2424 (5.3) | 48 (0.1) | 2 (0) | 7351 (16.2) |
| Scattered fibroglandular densities | 1918 (4.2) | 16 409 (36.2) | 2820 (6.2) | 76 (0.2) | 21 223 (46.8) |
| Heterogeneously dense | 96 (0.2) | 3866 (8.5) | 9384 (20.7) | 748 (1.7) | 14 094 (31.1) |
| Extremely dense | 7 (0) | 99 (0.2) | 1249 (2.8) | 1290 (2.8) | 2645 (5.8) |
| Total | 6898 (15.2) | 22 798 (50.3) | 13 501 (29.8) | 2116 (4.6) | 45 313 (100.0) |
| **Women with mammograms interpreted by different radiologists** | | | | | |
| Almost entirely fat | 3321 (9.7) | 1969 (5.7) | 43 (0.1) | 2 (0) | 5335 (15.6) |
| Scattered fibroglandular densities | 1617 (4.7) | 12 047 (35.2) | 2319 (6.8) | 69 (0.2) | 16 052 (46.8) |
| Heterogeneously dense | 82 (0.2) | 3302 (9.6) | 6872 (20.1) | 606 (1.8) | 10 862 (31.7) |
| Extremely dense | 5 (0) | 87 (0.3) | 1057 (3.1) | 873 (2.5) | 2022 (5.9) |
| Total | 5025 (14.7) | 17 405 (50.8) | 10 291 (30.0) | 1550 (4.5) | 34 271 (100.0) |
| **Women with mammograms interpreted by the same radiologist** | | | | | |
| Almost entirely fat | 1556 (14.1) | 455 (4.1) | 5 (0) | 0 (0) | 2016 (18.3) |
| Scattered fibroglandular densities | 301 (2.7) | 4362 (39.5) | 501 (4.5) | 7 (0.1) | 5171 (46.8) |
| Heterogeneously dense | 14 (0.1) | 564 (5.1) | 2512 (22.7) | 142 (1.3) | 3232 (29.3) |
| Extremely dense | 2 (0) | 12 (0.1) | 192 (1.7) | 417 (3.8) | 623 (5.6) |
| Total | 1873 (17.0) | 5393 (48.8) | 3210 (29.1) | 566 (5.1) | 11 042 (100.0) |

* Values are numbers (percentages). Percentages may not sum to totals due to rounding.

woman on the basis of her reported breast density. Although patient–provider discussions of supplemental screening may be triggered by mandatory reporting of density information, physicians should consider density information as only one subjective factor among many relevant risk factors that should be incorporated into decision making about screening. Policymakers should be aware that density assessment as currently practiced is subjective and highly variable across radiologists. Density reporting laws that suggest consideration of supplemental screening for women with dense breasts should include language acknowledging that density is a subjective measure that should be considered in the wider context of factors that influence the likelihood of a false-negative mammography result and future breast cancer risk. Of note, women who have dense breasts but are otherwise at low or average breast cancer risk do not have high false-negative rates on mammography (20). Various validated models are available for providers to characterize a patient's breast cancer risk (21–23). Additional evidence is urgently needed to support the development of guidelines for supplemental screening based on breast density and other established risk factors.

Our results illustrate the population-level effect of the moderate reliability in density assessment previously reported in earlier studies using test sets. A recent study using a test set of 282 mammograms interpreted by 19 radiologists found a mean $\kappa$ statistic of 0.46 for interradiologist agreement, with wide variation in the $\kappa$ statistic (ranging from 0.02 to 0.72) across radiologist pairs (16). Other test set studies have estimated $\kappa$ statistics ranging from 0.43 to 0.58 for interradiologist agreement (13, 14). Test set studies have also shown that intraradiologist agreement is higher ($\kappa$ statistic of approximately 0.70) than interradiologist agreement (13, 16). Of note, interradiologist agreement was also poorer than intraradiologist agreement in our study, and most women in our study with multiple mammograms during the study period had them interpreted by different radiologists.

Our complementary approach sought to compare the distribution of breast density assessments across radiologists in clinical practice. We focused particularly on variation in the percentage of patients characterized as having dense or nondense breasts because this dichotomization is linked to mandatory density notification laws now enacted in about half of U.S. states. The fraction of patients with dense breasts varied widely across radiologists, ranging from 6.3% to 84.5%. The middle 50% of radiologists varied by at least 20 percentage points in the proportion of patients rated as having dense breasts, even after adjustment for patient factors. Of note, there was less variation in the use of the extremely dense category. On the basis of our results, providers and policymakers may wish to distinguish between these categories, given that women with extremely dense breasts are most likely to be consistently rated as having dense breasts.

Our analyses of consecutive examinations demonstrate the magnitude of discordance when women have mammograms interpreted by different radiologists within a short period. No prior studies of clinically recorded density assessments from consecutive examinations have reported density concordance when limited to mammograms interpreted by different radiologists. One study included data from 87 066 women undergoing digital mammography (average of 483 days between examinations) at facilities within the Breast Cancer Surveillance Consortium (17). A $\kappa$ statistic of 0.54 was estimated for agreement between the consecutive density measures, although this included a mix of mammogram pairs that were interpreted by either the same radiologist or different ones. A prior study limited to consecutive mammograms ($n$ = 11 755 women) interpreted by the same radiologist within a 2-year period observed an overall $\kappa$ statistic of 0.59 for intraradiologist agreement (15). Our results show that with an average of just over 1 year between examinations, more than 1 in 6 women change density status if the mammograms are interpreted by different radiologists. The biological change in breast density over 1 year is expected to be small, with quantitative tools estimating a 1% decrease, on average, in breast density per year (24, 25). Of note, the discordance in density assessment in our study included differential classification in both directions (downgrading and upgrading).

The American College of Radiology and other organizations have highlighted the lack of reproducibility of breast density assessment in a statement cautioning about the potential unintended harms of mandatory breast density notification to patients (26). Our results provide further evidence of the need for objective, standardized measures of breast density. Several automated software programs have been developed for density quantification (27); these provide highly reproducible (28) and objective measures of density, typically on a continuous scale from 0% to 100%. Further research is needed to examine whether such automated tools can identify women who would benefit from supplemental breast cancer screening in addition to mammography.

Our study was limited to assessments by radiologists practicing in the clinical networks of the 3 PROSPR breast cancer screening research centers. Although these included a large number of academic and community practice breast imaging facilities in 4 states, the degree of variation in breast density assessment may differ in other clinical settings around the country. We observed greater variation in density assessment among radiologists within the Vermont PROSPR Research Center, which likely reflected the predominance of small community hospital radiology facilities served by generalist radiologists in the statewide Vermont PROSPR network. The PROSPR consortium is currently collecting additional information on radiology facility characteristics to evaluate predictors of variation in density assessment. Of note, all mammograms included in this study were interpreted before enactment of density notification legislation in the 4 included states. A recent single-institution study showed a trend among radiologists to downgrade breast density assessments immediately after the implementation of their state's breast density notification legislation, suggesting additional subjectivity (29). The potential effect of these laws on the degree of variation in density assessment is unknown. Finally, it is unclear whether the emerging adoption of digital breast tomosynthesis for breast cancer screening will affect breast density assessment, particularly among practices that abandon concomitant 2-dimensional digital mammography in favor of synthetic 2-dimensional images created from the reconstructed tomosynthesis views.

The overall distribution of breast density in our study population was similar to that reported in a prior large national study (8). Our study population had a lower rate of overweight and obesity (61% of those with known BMI) than in the U.S. population (68.6% [30]), which is consistent with the typically healthier cancer screening population. Our study included a proportion of African American women similar to that in the U.S. population but a higher percentage of non-Hispanic white women and a smaller fraction of Hispanic and Asian women. Variation in density assessment may differ at radiology practices serving a different demographic mix of patients, particularly if they serve a large proportion of Asian patients.

Our study was limited in that quantitative density measures were not available for comparison with the radiologist's subjective assessment. Rather, we used multivariable statistical models to account for variation across radiologists in patient case mix defined by age, race, and BMI. Age and BMI are the strongest known determinants of mammographic breast density (8, 31), and Asian women have elevated breast density that persists after adjustment for age and BMI (32). Other factors for which we did not adjust, including postmenopausal hormone use and reproductive history, have been associated with breast density, but their effects are modest compared with those of age and BMI (33). We found that adjustment for age, race, and BMI had little effect on the degree of variation in breast density assessment across radiologists. Adjustment for additional patient factors that have modest association with density, low population prevalence, or both (such as postmenopausal hormone use) is unlikely to substantially change our results. Finally, we note that our results likely reflect not only variation in radiologist interpretation of images but also the variation in the mammography machines and software used to produce digital mammographic images that is routinely present across and within facilities over time in clinical practice.

As the research and clinical communities seek to develop more reliable means of assessing breast density and identifying women in need of supplemental screening, our findings suggest that women, clinicians, and policymakers should consider the substantial variability in density assessment when considering screening options or risk stratification based on density information. Our results may also be useful as comparison data for radiologists reviewing their density assessment practice, analogous to what is available for assessing recall rate, cancer detection rate, and other breast imaging statistics within the range of values across peers (12, 34). Radiologists at the extremes of the distribution we report may wish to review the BI-RADS guidance for characterizing breast tissue composition. As breast density is increasingly used in screening decision making, the development of further professional standards, potentially including increased training or use of automated density quantification tools, may lead to more effective clinical care.

From University of Vermont, Burlington, Vermont; Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania; Geisel School of Medicine at Dartmouth, Lebanon, New Hampshire; Fred Hutchinson Cancer Research Center and Cancer Research and Biostatistics, Seattle, Washington; and Massachusetts General Hospital and Brigham and Women's Hospital, Boston, Massachusetts.

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**Reproducible Research Statement:** *Study protocol:* Not available. *Statistical code:* Available from Dr. Barlow (e-mail, williamb@crab.org). *Data set:* Individual data are not available, but research collaboration on this topic may be possible by contacting Dr. Barlow (e-mail, williamb@crab.org).

**Requests for Single Reprints:** Brian L. Sprague, PhD, Office of Health Promotion Research, University of Vermont, 1 South

Prospect Street, UHC Room 4425, Burlington, VT 05401; e-mail, Brian.Sprague@uvm.edu.

Current author addresses and author contributions are available at www.annals.org.

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**Current Author Addresses:** Dr. Sprague: Office of Health Promotion Research, University of Vermont, 1 South Prospect Street, UHC Room 4425, Burlington, VT 05401.
Drs. Conant and Schnall: Department of Radiology, Perelman School of Medicine, University of Pennsylvania, 1 Silverstein, 3400 Spruce Street, Philadelphia, PA 19104.
Drs. Onega and Tosteson: The Dartmouth Institute for Health Policy and Clinical Practice, Geisel School of Medicine at Dartmouth, 1 Medical Center Drive (HB7505), Lebanon, NH 03756.
Mr. Garcia: Fred Hutchinson Cancer Research Center, M3-C102, 1100 Fairview Avenue North, Seattle, WA 98109.
Dr. Beaber: Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, 1100 Fairview Avenue North, Seattle, WA 98109.
Dr. Herschorn: Department of Radiology, University of Vermont Medical Center, 111 Colchester Avenue, Burlington, VT 05401.
Dr. Lehman: Radiological Associates, Massachusetts General Hospital, 15 Parkman Street, Boston, MA 02114.
Dr. Lacson: Center for Evidence-Based Imaging, Department of Radiology, Brigham and Women's Hospital, 20 Kent Street, Brookline, MA 02445.
Dr. Kontos: Department of Radiology, Perelman School of Medicine, University of Pennsylvania, Room D702, Richards Building, 3700 Hamilton Walk, Philadelphia, PA 19104.
Dr. Haas: Division of General Internal Medicine and Primary Care, Brigham and Women's Hospital, 1620 Tremont Street, Boston, MA 02115.
Dr. Weaver: Department of Pathology, University of Vermont College of Medicine, Given Courtyard, 89 Beaumont Avenue, Burlington, VT 05405-0068.
Dr. Barlow: Cancer Research and Biostatistics, 1730 Minor Avenue, Suite 1900, Seattle, WA 98101.

**Author Contributions:** Conception and design: B.L. Sprague, E.F. Conant, E.F. Beaber, S.D. Herschorn, C.D. Lehman, M.D. Schnall, J.S. Haas, D.L. Weaver, W.E. Barlow.
Analysis and interpretation of the data: B.L. Sprague, E.F. Conant, T. Onega, M.P. Garcia, E.F. Beaber, S.D. Herschorn, C.D. Lehman, A.N.A. Tosteson, R. Lacson, D. Kontos, D.L. Weaver, W.E. Barlow.
Drafting of the article: B.L. Sprague, E.F. Conant, M.P. Garcia, R. Lacson, J.S. Haas, W.E. Barlow.
Critical revision of the article for important intellectual content: B.L. Sprague, E.F. Conant, T. Onega, M.P. Garcia, E.F. Beaber, S.D. Herschorn, C.D. Lehman, A.N.A. Tosteson, R. Lacson, D. Kontos, J.S. Haas, D.L. Weaver, W.E. Barlow.
Final approval of the article: B.L. Sprague, E.F. Conant, T. Onega, M.P. Garcia, E.F. Beaber, S.D. Herschorn, C.D. Lehman, A.N.A. Tosteson, R. Lacson, M.D. Schnall, D. Kontos, J.S. Haas, D.L. Weaver, W.E. Barlow.
Provision of study materials or patients: E.F. Conant, T. Onega, J.S. Haas.
Statistical expertise: M.P. Garcia, R. Lacson, W.E. Barlow.
Obtaining of funding: B.L. Sprague, E.F. Conant, T. Onega, A.N.A. Tosteson, M.D. Schnall, D. Kontos, J.S. Haas, D.L. Weaver, W.E. Barlow.
Administrative, technical, or logistic support: M.D. Schnall, J.S. Haas, D.L. Weaver.
Collection and assembly of data: B.L. Sprague, E.F. Conant, T. Onega, M.P. Garcia, S.D. Herschorn, R. Lacson, J.S. Haas, D.L. Weaver, W.E. Barlow.

## Appendix: Contributing PROSPR Investigators and Research Staff

The following investigators and staff at the PROSPR sites contributed to this work but did not author the manuscript, unless otherwise noted.

### Fred Hutchinson PROSPR Statistical Coordinating Center

Principal Investigators: William Barlow, PhD*, and Mark Thornquist, PhD (former Principal Investigator: Ziding Feng, PhD)

Co-investigators: Andrea Burnett-Hartman, PhD; John Inadomi, MD; Constance Lehman, MD*; Chris Li, PhD; Constance Mao, MD; Rachel Winer, PhD; and Yingye Zheng, PhD

Management: Stephanie Page-Lester and Suzanna Reid, PhD

Staff: Hallie Pritchett, MPH, and Kiarra Witcher, MPH-c

Data: Elisabeth Beaber, PhD, MPH*; Michael Garcia, MS*; Dale McLerran, MS; Janeira St. Clare; Deanna Stelling; and Greg Warnick

### UPenn Breast PROSPR Research Center

Principal Investigators: Katrina Armstrong, MD, MSCE, and Mitchell Schnall, MD, PhD*

Co-investigators: Jinbo Chen, PhD; Emily Conant, MD*; Despina Kontos, PhD*; Marilyn Schapira, MD, MPH; and Marie Synnestvedt, PhD

Management: Mirar Bristol, MA, and Carrie Inge, MPH

Staff: Ahmed Ashraf, PhD; Nigel S. Bristol; James Gee, PhD; Tory Harrington, BS; Dan Heitjan, PhD; Steve Honeywell, BS; Robert Hornik, PhD; Jordan Kahle, BA; Brad Keller, PhD; Joseph Cappella, PhD; Andrew Maidment, PhD; Anne Marie McCarthy, PhD; Michael Meng-Kang Hsieh, MS; Nandita Mitra, PhD; Andrew Oustimov, MS; Lauren Pantalone, BS; Holli Seitz, MPH, PhD Candidate; Shonket Ray, PhD; Christine Skubisz, PhD; and Yuanjie Zheng, PhD

### Vermont Breast PROSPR Research Center

Principal Investigators: Brian L. Sprague, PhD*, and Donald L. Weaver, MD* (former Principal Investigator: Berta M. Geller)

Co-investigators: Oguzhan A. Alagoz, Kim L. Dittus, Kevin W. Eliceiri, Mark F. Evans, Berta M. Geller, Andrew J. Goodwin, Sally D. Herschorn*, Patricia J. Keely, John A. Shepherd, Joan M. Skelly, Natasha K. Stout, Amy Trentham-Dietz, Pamela M. Vacek, and Brenda L. Waters

Management: Mark Bowman, Kathleen Howe, and Dawn Pelkey

Staff: Rachael Chicoine, Meghan Farrington, Cindy Groseclose, Victoria Hart, John Mace, Denis Nunez, Tiffany Pelkey, Dusty Quick, Oyewale Shiyanbola, and Christopher Veal

### Dartmouth-Brigham Breast PROSPR Research Center

Principal Investigators: Jennifer S. Haas, MD, MS*; Tracy Onega, PhD*; and Anna N.A. Tosteson, ScD*

Co-investigators: Robyn Birdwell, MD; Ramin Khorasani, MD, MPH; Ronilda Lacson, MD, PhD*; Elissa Ozanne, PhD; and Tor D. Tosteson, ScD

Clinical Advisors: Asaf Bitton, MD, MPH; Charles Brackett, MD; Roberta di Florio, MD; Joel Lazar, MD; and Wendy Wells, MD

Study Staff: Mackenzie Bronson, BA; Jane Chen, BS; Martha Goodrich, MS; Kimberly A. Harris, MM; Stella St. Hubert, AB; and Loretta Pearson, MPhil

Data: Steven Andrews; Kristen Anton, MS; Katrine Batcho, CTR; Phyllis Brawarsky, MPH; Charles Cook, BS; Amar Das, MD, PhD; Ryan Dougher; Scottie Eliassen, MS; Scott Farr, BA; Carol Felone; Tracy Frazee; Scott Gerlach, BA; George Getty, BS; John Gilman, BS; Dick Hanson, BA; Dennis Johnson; Brenda Joseph; Leslie A. Laam, MS; Brian Levin; Meg Menkov, BA; Steven Pyle, MSE; Laura Sims-Larabee, BS, CTR; Ingrid Stendhal, RHIA, CTR; Carol Venuti, RHIA, CTR; Julie Weiss, MS; and Deborah Williams, MA

Scientific Advisors: David Bates, MD, MPH; Graham Colditz, MD; and Harold Sox, MD

### Group Health Research Institute Colorectal PROSPR Research Center

Principal Investigators: Jessica Chubak, PhD, and Aruna Kamineni, PhD, MPH

Co-investigators: Diana S.M. Buist, PhD, MPH; Beverly B. Green, MD, MPH; Christopher L. Owens, MD; Carolyn M. Rutter, PhD; and Karen Wernli, PhD

Management: Gabrielle Gundersen and Kristina Hansen

Staff: Vina Graham; Kevin P. Filocamo; Ann Kelley, MHA; Kilian Kimbel; Steve Koets, RN; Jennifer Macuiba, MS, MHA; Melissa Rabelhofer; Renee Remedios; and Leslie Sizemore

Data: Hongyuan Gao, MS; Scott Halgrim, MA; Eric Johnson, MS; Lawrence Madziwa, MS; Malia Oliver; Chester Pabiniak, MS; and Diem-Thy Tran

### Parkland-UT Southwestern Colorectal PROSPR Research Center

Principal Investigators: Ethan A. Halm, MD, MPH; Celette Sugg Skinner, PhD; and Jasmin A. Tiro, PhD, MPH

Co-investigators: Chul Ahn, PhD; Ruben Amarasingham, MD, MBA; Bijal Balasubramanian, MBBS, PhD; Stephen Inrig, PhD; Simon Craddock Lee, PhD, MPH; Milton Packer, MD; Sandi Pruitt, PhD; Noel Santini, MD; Isabel Scarinci, PhD, MPH; Amit Singal, MD, MSCS; Claudia Werner, MD; and Rachel Winer, PhD

Management: Wendy Bishop, MS, and Katharine McCallister

Data: Eric Borton, MS; Adam Loewen; and Joanne Sanders, MS

Consultant: Samir Gupta, MD

### Kaiser Permanente Research Institute Colorectal PROSPR Research Center

#### *Kaiser Permanente Northern California*

Principal Investigators: Douglas A. Corley, MD, PhD; Chyke A. Doubeni, MD, MPH (University of Pennsylvania); Michael J. Silverberg, PhD, MPH; and Ann G. Zauber, PhD (Memorial Sloan Kettering Cancer Center)

Co-investigators: Theodore R. Levin, MD; Tina R. Raine-Bennett, MD, MPH; and George F. Sawaya, MD (University of California, San Francisco)

Management: Christopher D. Jensen, PhD, MPH

Data: Natalia Udaltsova, PhD, and Wei K. Zhao, MPH

#### *Kaiser Permanente Southern California*

Principal Investigator: Chun R. Chao, PhD, MS, and Virginia P. Quinn, PhD, MPH

Co-investigators: Alexander T. Lee, MD; Neal M. Lonky, MD, MPH; and Joanne E. Schottinger, MD

Management: Tracy A. Becerra, PhD, MPH, and Nirupa R. Ghai, PhD, MPH

Data: Richard Contreras, MS, and Angela Li, MS

### New Mexico HPV Outcomes, Practice Effectiveness, and Surveillance (NM-HOPES) Cervical PROSPR Research Center

Principal Investigator: Cosette M. Wheeler, PhD

Co-investigators: Philip Castle, PhD, MPH; Jack Cuzick, PhD; Daniel Goldberg, PhD; Jane J. Kim, PhD; Isabel Scarinci, PhD; Alan Waxman, MD, MPH; and Charles Wiggins, PhD

Management: Lee Fernando and Ann Powell, MBA

Staff: Nicole G. Campos, PhD; Eloisa Chavez; Jamilah Gamougoun, BA; Verna Newman, AA; Nikhil Patel, MD, MPH; and Jeannie Maurice, BS

Data: Scott Horlbeck, BA; William C. Hunt, BA; Ruth McDonald, MS; Orrin Myers, PhD; Michael Robertson, BS; and Stephen Sy, BS

Executive Leadership Group: Philip Castle, PhD, MPH; Jack Cuzick, PhD; Jane J. Kim, PhD; Isabel Scarinci, PhD; Alan Waxman, MD, MPH; Cosette M. Wheeler, PhD; and Robert Williams, MD

### Group Health Research Institute Cervical PROSPR Research Center

Principal Investigators: Jessica Chubak, PhD, and Aruna Kamineni, PhD, MPH

Co-investigators: Diana S.M. Buist, PhD, MPH, and Christopher L. Owens, MD

Management: Gabrielle Gundersen

Staff: Vina Graham; Steve Koets, RN; Jennifer Macuiba, MS, MHA; and Melissa Rabelhofer

Data: Hongyuan Gao, MS; Lawrence Madziwa, MS; and Malia Oliver

## Parkland-UT Southwestern Cervical PROSPR Research Center

Principal Investigators: Celette Sugg Skinner, PhD, and Jasmin A. Tiro, PhD, MPH

Co-investigators: Bijal Balasubramanian, MBBS, PhD; Ethan A. Halm, MD, MPH; Stephen Inrig, PhD; Sandi Pruitt, PhD; Noel Santini, MD; Isabel Scarinci, PhD, MPH; Claudia Werner, MD; and Rachel Winer, PhD

Management: Wendy Bishop, MS

Data: Eric Borton, MS, and Joanne Sanders, MS

## Kaiser Permanente Research Institute Cervical PROSPR Research Center

### *Kaiser Permanente Northern California*

Principal Investigators: Douglas A. Corley, MD, PhD, and Michael J. Silverberg, PhD, MPH

Co-investigators: Tina R. Raine-Bennett, MD, MPH, and George F. Sawaya, MD (University of California, San Francisco)

Management: Christopher D. Jensen, PhD, MPH

Data: Natalia Udaltsova, PhD, and Wei K. Zhao, MPH

### *Kaiser Permanente Southern California*

Principal Investigator: Chun R. Chao, PhD, MS

Co-investigators: Neal M. Lonky, MD, MPH; Virginia P. Quinn, PhD, MPH; and Joanne E. Schottinger, MD

Management: Tracy A. Becerra, PhD, MPH

Data: Richard Contreras, MS, and Angela Li, MS

## National Cancer Institute

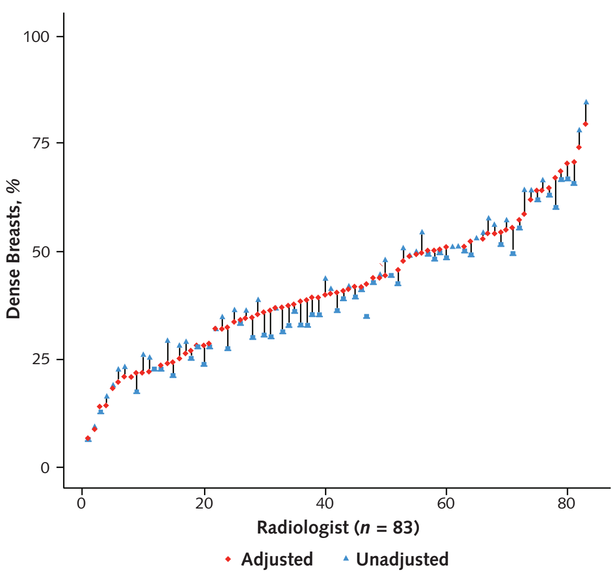
Project Scientists: Stephen Taplin, MD, MPH (*lead*); Sarah Kobrin, PhD, MPH; and V. Paul Doria-Rose, DVM, PhD

Program Director: Tonya Parker

Program Manager: Cheryl DeAguiar

* Authored the manuscript.

***Appendix Figure.*** Paired unadjusted and multivariable-adjusted percentage of patients with dense breasts (heterogeneously or extremely dense), by radiologist.




For each radiologist, a black line connects the unadjusted percentage with dense breasts (*blue triangle*) to the percentage with dense breasts after adjustment for patient age, race/ethnicity, and body mass index (*red diamond*). Examinations with missing race/ethnicity and body mass index were excluded from both the unadjusted and multivariable-adjusted results.